| ABS | Study design | Year | Author | Title | Study population | Clinical outcome | Significant association | Evidence level | Quality | Delirium | Cognition | Mortali | ty Fall |
|-----|-------------------------------|------|-------------------|--|---|--|-------------------------|-------------------------|---------------------|----------|-----------|---------------|---------|
| AAS | Cohort study | - | Ehrt et al. | Use of drugs with anticholinergic effect and impact on | Community-based PD patients, | Cognitive function (MMSE) | + | (adapted EBM Oxford) 2a | (NOS, RoB 2.0) Good | 0 | 1 | 0 | 0 |
| | | | | cognition in Parkinson's disease: a cohort study | $n = 235$ with a mean age of 74.7 ± 8.4 years | Hospital admissions | + | | | | | | |
| AAS | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, n = $537'387$ with a mean age of 74.7 ± 7.6 years | Falls-related hospitalizations LOS GP visits | + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| ABC | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| ABC | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | - - - | 5 | Poor | 0 | 1 | 0 | 1 |
| ACB | Cohort study | 2010 | Campbell et al. | Use of anticholinergics and the risk of cognitive impairment in an African American population | Community-dwelling African American, $n = 1652$ mean age of 81.8 ± 5.3 years | Cognitive Impairment | + | 2a | Good | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2011 | Campbell et al. | Association between prescribing of anticholinergic medications and incident delirium: a cohort study | Hospitalized patients with cognitive impairment, $n = 147 \text{ aged} \ge 65 \text{ years}$ | Delirium (CAM) | - | 4 | Poor | 1 | 0 | 0 | 0 |
| ACB | Cohort study | 2011 | Fox et al. | The impact of anticholinergic burden in Alzheimer's Dementia-the Laser-AD study | Nursing & residual homes, in- and outpatients with Alzheimer dementia (AD), $n = 224$ with a mean age of 81 ± 7.4 years, | Cognitive function (MMSE, SIB, ADAS-COG score) | - | 2a | Good | 0 | 1 | 0 | 0 |
| АСВ | Cohort study (multicenter) | 2011 | Fox et al. | Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study | In- and outpatients with complete MMSE score and medication, $n = 12'250$ aged ≥ 65 years | Cognitive function (MMSE) Mortality | + + | 2a | Good | 0 | 1 | 1 | 0 |
| АСВ | Cohort study | 2013 | Koyama et al. | Ten-year trajectory of potentially inappropriate medications in very old women: importance of cognitive status | Community-dwelling women, $n=1484$, at baseline with $n=358$ users with a mean age of 78 ± 3.1 years and $n=1115$ non-users with a mean age of 78 ± 3.2 years | Cognitive function (MCI) Dementia | + + | 4 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2013 | Mangoni et al. | Measures of Anticholinergic Drug Exposure, Serum Anticholinergic Activity, and All-cause Post discharge Mortality in Older Hospitalized Patients with Hip Fractures | Patients with hip fractures and planned surgery, $n = 71$ with a mean age of 84 ± 6 years | Postoperative complications LOS 3 month all-cause mortality 1 year all-cause mortality | - - - | 2a | Good | 0 | 0 | 1 | 0 |
| АСВ | Cohort study | 2014 | Kashyap et al. | Methodological Challenges in Determining Longitudinal Associations Between Anticholinergic Drug Use and Incident Cognitive Decline | Outpatient clinics without dementia or depression, $n = 102$ with a mean age 71.9 ± 7.3 of years | Cognitive function (MMSE, GDP) | + | 4 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cohort study (multicenter) | 2014 | Kidd et al. | The relationship between total anticholinergic burden (ACB) and early in-patient hospital mortality and length of stay in the oldest old aged 90 years and over admitted with an acute illness | Inpatients, $n = 419$ with a median age of 92.9 years, ACB 0: $n = 163$ with a median age of 93.4 years ACB 1: $n = 142$ with a median age of 92.9 years ACB ≥ 2 : $n = 114$ with a median age of 92.5 years | Mortality LOS | - | 2b | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study (multicenter) | 2014 | Koyama et al. | Long-term cognitive and functional effects of potentially inappropriate medications in older women | Community-dwelling women, $n = 1429$ with a mean age of 83.2 ± 3.3 years | Functional outcome (IADL) Cognitive function (MMSE) | + | 4 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2015 | Myint et al. | Total anticholinergic burden and risk of mortality and cardiovascular disease over 10 years in 21,636 middle-aged and older men and women of EPIC-Norfolk prospective population study | Community-dwelling patients without cancer, $n=21'636$ ACB 0: $n=17'317$ with a mean age of 57.9 ± 9.1 years ACB 1: $n=2704$ with a mean age of 62.9 ± 8.8 years ACB 2-3: $n=1324$ with a mean age of 62.2 ± 9.2 years ACB ≥ 3 : $n=291$ with a mean age of 63.1 ± 8.9 years | All-cause mortality Incident CVD | ++++ | 2b | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2015 | Richardson et al. | Use of Medications with Anticholinergic Activity and Self- Reported Injurious Falls in Older Community-Dwelling Adults | Community-dwelling patients without dementia, $n = 2696 \text{ aged} \ge 65 \text{ years, men (m) } n = 1286 \text{ and}$ women (w) $n = 1410$ | Injurious falls (m/f) Any falls (m/f) Total number of falls (m/f) | +/- -/- -/- | 2a | Good | 0 | 0 | 0 | 1 |
| ACB | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 \pm 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| АСВ | Cohort study | 2016 | Campbell et al. | Association of Anticholinergic Burden with Cognitive Impairment and Health Care Utilization Among a Diverse Ambulatory Older Adult Population | Community-dwelling patients, $n = 3344 \text{ aged} \ge 65 \text{ years}$ | Cognitive impairment Inpatient, ED and outpatient visit | + + | 2b | Good | 0 | 1 | 0 | 0 |
| АСВ | Cohort study | 2016 | Vetrano et al. | Anticholinergic Medication Burden and 5-Year Risk of Hospitalization and Death in Nursing Home Elderly Residents With Coronary Artery Disease | Nursing home residents, $n = 3781$ with a mean age of 83 ± 7 years | Hospitalization Mortality | + + | 2b | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2017 | Cossette et al. | Association Between Anticholinergic Drug Use and Health- Related Quality of Life in Community-Dwelling Older Adults | Community-dwelling patients free of disabilities in ADL and cognitive impairment, $n = 1793$ with a mean age of 74.4 ± 4.2 years | Mental Component Summary (MCS) Physical Component Summary (PCS) | + | 4 | Poor | 0 | 1 | 0 | 0 |

| | | | | mpact on clinical outcomes - a systematic review, EJCP, Liseach anticholinergic burden scale (ABS) (total n=147). | sibach A et al, Corresponding author: Pr Chantal Csajl | ta, Center for Research and Innovation in Clinical P | harmaceutical Sciences, | Rue du Bugnon 17, 10 | 05 Lausanne | | | | |
|-----|---|--------|-----------------------|---|--|---|---|--|---------------------------|----------|-----------|----------|---------|
| ABS | Study design | | Author | Title | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | y Falls |
| ACB | Cohort study (multicenter) | 2017 | Cross et al. | Potentially Inappropriate Medication, Anticholinergic Burden, and Mortality in People Attending Memory Clinics | Community-dwelling patients with mild cognitive impairment or dementia of 9 memory clinics, $n = 964$ with a mean age of 77.6 ± 7.4 years | Mortality | + | 2a | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2017 | Egberts et al. | Anticholinergic drug exposure is associated with delirium and post discharge institutionalization in acutely ill hospitalized older patients | Acutely ill, hospitalized patients (> 3 days), n = 905 with a mean age of 81.0 ± 7.03 years | Delirium on admission LOS Postdischarge institutionalization In hospital mortality | - - - | 2b | Good | 1 | 0 | 1 | 0 |
| ACB | Cohort study | 2017 | Naharci et al. | Effect of anticholinergic burden on the development of dementia in older adults with subjective cognitive decline | Patients with subjective cognitive decline, $n = 109$ with a mean age 72.5 ± 63 years | Dementia | + | 2b | Good | 0 | 0 | 0 | 0 |
| ACB | Cohort study | 2017 | Wen-Han Hsu et al. | Comparative Associations Between Measures of Anti- cholinergic Burden and Adverse Clinical Outcomes | Inpatients n = 116'043 aged > 65 years | Emergency Department Visits All-Cause Hospitalizations Fracture-Specific Hospitalization Incident dementia | + + + (specific age group) + (in pat. 65-74 y. only) | 2b | Good | 0 | 0 | 0 | 0 |
| ACB | Cohort study | 2018 | Brombo et al. | Association of Anticholinergic Drug Burden with Cognitive and Functional Decline Over Time in Older Inpatients: Results from the CRIME Project | Inpatients $n = 1123$ with a mean age of 81 ± 7.5 years | Cognitive status (MMSE) Functional status (ADL) | + + | 4 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2018 | Campbell et al. | Anticholinergics Influence Transition from Normal Cognition to Mild Cognitive Impairment in Older Adults in Primary Care | Community-dwelling people, $n = 350$ with a mean age of 71.2 ± 5.1 years | Transition from normal to MCI in patients w/o dementia | + | 2a | Good | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2018 | Gamble et al. | Baseline anticholinergic burden from medications predicts incident fatal and non-fatal stroke in the EPIC-Norfolk general population | Outpatients, $n = 21'722$ with a mean age of 58.9 ± 9.2 years | Incident stroke Stroke mortality | ++ | 2b | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study (in an intervention study) | n 2018 | Jaïdi et al. | Threshold for a Reduction in Anticholinergic Burden to Decrease Behavioral and Psychological Symptoms of Dementia | Inpatients with dementia and hospitalized for behavioral and psychological symptoms (BPSD), $n=147$ with a mean age of 84.1 ± 5.2 years | Clinical and statistical significant improvement in BPSD when ACH load is reduced | - | 2a | Good | 0 | 0 | 0 | 0 |
| ACB | Cohort study (multicenter) | 2018 | Lattanzio et al. | Anticholinergic burden and 1-year mortality among older patients discharged from acute care hospital | Patients discharged from acute care hospitals, $n = 807$ with a mean age of 81.0 ± 7.4 years | Mortality | + | 2a | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2018 | Tan et al. | Anticholinergic burden and risk of stroke and death in people with different types of dementia | Patients with different dementia subtypes, $n = 39'107$ with a mean age of 79.9 ± 7.9 years | Stroke All-cause mortality | + | 2b | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2018 | Ziad et al. | Anticholinergic drug use and cognitive performances in middle age: findings from the CONSTANCES cohort | Participants living in France, n = 34'267 aged 45-70 years | Cognitive performance (episodic memory, verbal fluency, executive functions) | - | 2b | Good | 0 | 1 | 0 | 0 |
| ACB | Cohort study | 2019 | Ah et al. | Effect of anticholinergic burden on treatment modification, delirium and mortality in newly diagnosed dementia patients starting a cholinesterase inhibitor: A population-based study | Patients with cholinesterase inhibitor treatment for dementia, $n = 7438$ aged > 60 years $ACB \le 1$: $n = 5884$ $ACB > 3$: $n = 1554$ | Delirium (ICD-10 F5.0) Mortality | + | 2b | Good | 1 | 0 | 1 | 0 |
| ACB | Cohort study (reanalysis on a RCT) | 2019 | Andre et al. | Anticholinergic exposure and cognitive decline in older adults: effect of anticholinergic exposure definitions in a 3-year analysis of the multidomain Alzheimer preventive trial (MAPT) study | Community-dwelling French adults, $n=1396 \text{ with a mean age of } 75.2 \pm 4.4 \text{ years}$ | Cognitive decline (assessed with a composite score following MMSE, Free and Cued Selective Reminding Test, Category Naming Test, Digit Symbol Substitution Test) | - | 2a | Good | 0 | 1 | 0 | 0 |
| ACB | Cohort study (multicenter) | 2019 | Corsonello et al. | The excess mortality risk associated with anticholinergic burden among older patients discharged from acute care hospital with depressive symptoms | Hospitalized patients in 7 acute care centers, $n = 576$ with a mean age of 79.6 ± 7.0 years | Mortality at 1-year after discharge | + | 2a | Good | 0 | 0 | 1 | 0 |
| ACB | Cohort study | 2019 | Green et al. | Drugs Contributing to Anticholinergic Burden and Risk of Fall or Fall-Related Injury among Older Adults with Mild Cognitive Impairment, Dementia and Multiple Chronic Conditions: A Retrospective Cohort Study | Patients with impaired cognition, $n = 10'698$ with a mean age of 79.1 ± 7.99 years | Falls Falls related injuries | + | 2b | Good | 0 | 0 | 0 | 1 |
| АСВ | Cohort study (in a RCT) | 2019 | Joshi et al. | Verbal learning deficits associated with increased anticholinergic burden are attenuated with targeted cognitive training in treatment refractory schizophrenia patients | Schizophrenic patients, intervention group $n=24$ with a mean age of 34.54 ± 12.13 years and control group $n=22$ with a mean age of 35.73 ± 13.0 years | Learning verbal training in intervention group Learning verbal training in control group | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ACB | Cohort study | 2019 | Szabo et al. | Association between cumulative anticholinergic burden and falls and fractures in patients with overactive bladder: US-based retrospective cohort study | Outpatients with overactive bladder, n = 154'432 with a mean age of 55.7 years | Falls Fractures | + + | 2b | Good | 0 | 0 | 0 | 1 |
| АСВ | Nested Case- Control study | 2016 | Chatterjee et al. | Anticholinergic Medication Use and Risk of Fracture in Elderly Adults with Depression | Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), $n=352'937 \text{ with depression and no baseline fractures} \\ \text{or falls in 2007, incidence matched cohort} \\ n=202'260 \text{ with } n=161'808 \text{ controls and } n=40'452 \\ \text{cases, mean age of } 81.4 \pm 7.4 \text{ years} \\$ | Fracture risk | + | 3 | Good | 0 | 0 | 0 | 0 |
| ACB | Case-Control study | 2016 | Zia et al. | Anticholinergic burden is associated with recurrent and injurious falls in older individuals | Patients, $n = 263$ cases with a mean age of 75.3 ± 7.3 years and $n = 165$ controls with a mean age of 72.13 ± 5.5 years | Recurrent and injurious falls | - | 3 | Good | 0 | 0 | 0 | 1 |

| Quality of anticholinergic burden scales and their impact on clinical outcomes - a systematic review, EJCP, Lisibach A et al, Corresponding author: Pr Chantal Csajka, Center for Research and Innovation in Clinical Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Appendix 6a: Identified validations / evaluations for each anticholinergic burden scale (ABS) (total n=147). ABS Study design Year Author Title Study population Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Clinical outcome Significant association Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Company | | | | | | | | | | | | | |
|--|-------------------------------|------|--------------------------|--|---|--|---------------------------|----------------------|----------------|----------|-----------|----------|---------|
| | | | | , , , , , , | | | | Evidence level | Quality | | | | Τ |
| ABS | Study design | Year | Author | Title | Study population | Clinical outcome | Significant association | (adapted EBM Oxford) | (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | y Falls |
| ACB | Nested Case- Control study | 2018 | Richardson et al. | Anticholinergic drugs and risk of dementia: case-control study | Outpatients, aged \geq 65 years n = 40'770 cases and n = 283'933 controls (matching 1:7) | Incidence of dementia | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ACB | Cross-sectional | 2009 | Kolanowski et al. | A Preliminary Study of Anticholinergic Burden and Relationship to a Quality of Life Indicator, Engagement in Activities, in Nursing Home Residents With Dementia | Nursing home residents with dementia, $n = 87$ with a mean age of 85.7 ± 6.3 years | Quality of life: Multiple engagement observations | - | 5 | Good | 0 | 0 | 0 | 0 |
| ACB | Cross-sectional | 2013 | Pasina et al. | Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study | Hospitalized patients, $n = 1232$ with age of ≥ 65 years | Cognitive function (SBT) Physical function (BI) | + | 5 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cross-sectional | 2014 | Lanctot et al. | Assessing Cognitive Effects of Anticholinergic Medications in Patients With Coronary Artery Disease | Outpatients with coronary artery disease, $n = 131$ with a mean age of 64.2 ± 9.1 years | Attention, speed, executive function | + | 5 | Poor | 0 | 0 | 0 | 0 |
| ACB | Cross-sectional | 2016 | O'Dwyer et al. | Association of anticholinergic burden with adverse effects in older people with intellectual disabilities: an observational cross-sectional study | Patients with intellectual disability, $n = 736 \text{ aged} \ge 40 \text{ years}$ | Daytime dozing Constipation | + | 5 | Poor | 0 | 0 | 0 | 0 |
| ACB | Cross-sectional | 2017 | Ang et al. | The Impact of Medication Anticholinergic Burden on Cognitive Performance in People With Schizophrenia | Outpatients and inpatients with schizophrenia, $n = 705$ with a mean age of 39.18 ± 9.71 years | Cognitive performance (executive functions, fluency/memory, speed/vigilance) | - | 5 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cross-sectional | 2017 | Dauphinot et al. | Anticholinergic drugs and functional, cognitive impairment and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders | Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years | Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia) | + (MMSE, NPI) - (IADL) | 5 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + - + | 5 | Poor | 0 | 1 | 0 | 1 |
| ACB | Cross-sectional | 2017 | Pfistmeister et al. | Anticholinergic burden and cognitive function in a large German cohort of hospitalized geriatric patients | Hospitalized patients, $n = 89'579$ with a median age of 82 years, complete case analysis for cognitive impairment $n = 59'007$ and for dementia $n = 68'388$ | Cognitive Impairment (MMSE) Dementia | + | 5 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cross-sectional | 2017 | Tsoutsoulas et al. | Anticholinergic Burden and Cognition in Older Patients With Schizophrenia | Community-dwelling patients with schizophrenia or schizoaffective disorder, $n = 60$ with a mean age of 63.6 ± 6.83 years | Alzheimer's dementia-related cognitive functions | + | 5 | Poor | 0 | 1 | 0 | 0 |
| ACB | Cross-sectional | 2018 | Ablett et al. | A high anticholinergic burden is associated with a history of falls in the previous year in middle-aged women: findings from the Aberdeen Prospective Osteoporosis Screening Study | Community-dwelling women, $n = 3883$ with a mean age of 54.33 ± 2.27 years | History of falls | + | 5 | Poor | 0 | 0 | 0 | 1 |
| ACB | Cross-sectional | 2019 | Pasina et al. | Relation Between Delirium and Anticholinergic Drug Burden in a Cohort of Hospitalized Older Patients: An Observational Study | Inpatients, $n = 502$, with delirium $n = 151$ with a mean age of 85.0 ± 6.5 years and without delirium $n = 32$ with a mean age of 83.4 ± 6.5 years | Delirium (4 AT) | + | 5 | Poor | 1 | 0 | 0 | 0 |
| ACL | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| ACL | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + + + | 5 | Poor | 0 | 1 | 0 | 1 |
| ADS | RCT | 2013 | Kersten et al. | Cognitive effects of reducing anticholinergic drug burden in a frail elderly population: a randomized controlled trial | Nursing home residents, n = 87 with a mean age of 85 years | Cognitive function Mouth dryness | - | 1 | Good | 0 | 1 | 0 | 0 |
| ADS | Cohort study | 2009 | Low et al. | Use of medications with anticholinergic properties and cognitive function in a young-old community sample | Community-dwelling patients, $n = 2058$ with a mean age of 62.5 ± 1.5 years | Mild cognitive impairment | - | 2a | Good | 0 | 1 | 0 | 0 |
| ADS | Cohort study | 2012 | Gouraud-Tanguy et al. | Analysis of iatrogenic risk related to anticholinergic effects using two scales in acute geriatric inpatient unit | Patients from the geriatric care unit, $n = 1379$ with a mean age of 85 ± 6 years | Total anticholinergic side effects Peripheral anticholinergic side effects Central anticholinergic side effects | + + - | 4 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cohort study | 2013 | Mangoni et al. | Measures of Anticholinergic Drug Exposure, Serum Anticholinergic Activity, and All-cause Post discharge Mortality in Older Hospitalized Patients with Hip Fractures | Patients with hip fractures and planned surgery, $n = 71$ with a mean age of 84 ± 6 years | Postoperative complications LOS 3 month all-cause mortality 1 year all-cause mortality | - - - | 2a | Good | 0 | 0 | 1 | 0 |
| ADS | Cohort study | 2014 | Kalisch et al. | Multiple Anticholinergic Medication Use and Risk of Hospital Admission for Confusion or Dementia | Australian veterans, $n = 36'015$ with a mean age of 82.9 ± 6.8 years | Risk of hospitalization for confusion or dementia | + | 2b | Good | 0 | 0 | 0 | 0 |

| | | | | mpact on clinical outcomes - a systematic review, EJCP, Lis | ibach A et al, Corresponding author: Pr Chantal Csajk | ta, Center for Research and Innovation in Clinical P | harmaceutical Sciences, | Rue du Bugnon 17, 100 |)5 Lausanne | | | | |
|---------|---|-----------|---------------------------|--|--|---|-------------------------|--|---------------------------|----------|-----------|----------|-------------|
| Appendi | ix 6a: Identified va | lidations | s / evaluations for e | each anticholinergic burden scale (ABS) (total n=147). | | T | | <u> </u> | | | | | |
| ABS | Study design | Year | Author | Title | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | y Falls |
| ADS | Cohort study | 2014 | Kashyap et al. | Methodological Challenges in Determining Longitudinal Associations Between Anticholinergic Drug Use and Incident Cognitive Decline | Outpatient clinics without dementia or depression, $n = 102$ with a mean age of 71.9 ± 7.3 years | Cognitive function (MMSE, GDP) | + | 4 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cohort study | 2015 | Block et al. | The interaction between medical burden and anticholinergic cognitive burden on neuropsychological function in a geriatric primary care sample | Primary care patients (outpatients), n = 290 with a mean age of 72.76 ± 5.47 years | Neuropsychological functions (RBANS test) | - | 4 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cohort study | 2015 | Gupte et al. | Impact of anticholinergic load of medications on the length of stay of cancer patients in hospice care | Cancer patients discharge from hospice care, selected by ICD-9 codes 140 - 239 , $n = 1801$ ADS 0-2: $n = 641$, mean age of 72.38 ± 13.50 years ADS 3-5: $n = 637$, mean age of 71.75 ± 13.83 years ADS ≥ 6 : $n = 523$, mean age of 70.42 ± 13.79 years | LOS / survival in hospice care (US) | + | 2b | Good | 0 | 0 | 0 | 0 |
| ADS | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + | 2ь | Good | 0 | 0 | 0 | 1 |
| ADS | Cohort study | 2015 | Wolters et al. | Anticholinergic Medication Use and Transition to Delirium in Critically Ill Patients: A Prospective Cohort Study | Critically ill inpatients, $n = 1112$ with a mean age of 60 ± 16 years | Delirium onset (ICU-CAM) | - | 2a | Good | 1 | 0 | 0 | 0 |
| ADS | Cohort study | 2015 | Yarnall et al. | Anticholinergic Load: Is there a Cognitive Cost in Early Parkinson's Disease? | Community-dwelling and outpatients with Parkinson, ADS = 0: $n = 112$ with a mean age of 68.6 ± 8.9 years ADS ≥ 1 : $n = 84$ with a mean age of 69.7 ± 7.7 years | Mild cognitive impairment in Parkinson's disease | - | 4 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cohort study (reanalysis on a RCT) | 2016 | Hochman et al. | Anticholinergic Drug Burden in Noncancer Versus Cancer Patients Near the End of Life | Comparing patients with cancer $n=126$ with a mean age of 79.1 ± 10.6 years and without cancer $n=118$ with a mean age of 69.7 ± 10.5 years | Fatigue Quality of life (QOL) (worse) Drowsiness Well-being | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cohort study | 2017 | Cossette et al. | Association Between Anticholinergic Drug Use and Health- Related Quality of Life in Community-Dwelling Older Adults | Community-dwelling patients free of disabilities in ADL and cognitive impairment, $n=1793$ with a mean age of 74.4 ± 4.2 years | Mental Component Summary (MCS) Physical Component Summary (PCS) | - | 4 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cohort study (multicenter) | 2017 | Jean-Bart et al. | Exposure to anticholinergic and sedative medicines as indicators of high-risk prescriptions in the elderly | Inpatients, $n = 315$ with a mean age of 86.6 ± 6.2 years | Risk of falls | - | 2a | Good | 0 | 0 | 0 | 1 |
| ADS | Cohort study | 2017 | Sarbacker et al. | Total anticholinergic burden and survival within a cohort of elderly Mexican Americans | Mexican Americans, n = 1497 with a mean age of 74.56 years | Mortality | + | 2b | Good | 0 | 0 | 1 | 0 |
| ADS | Cohort study (for part of outcomes) | 2017 | Sevilla-Sanchez et al. | Adverse drug events in patients with advanced chronic conditions who have a prognosis of limited life expectancy at hospital admission | Inpatients requiring palliative care, $n = 235$ with a mean age of 86.8 ± 5.37 years | Survival | - | 2a | Good | 0 | 0 | 0 | 0 |
| ADS | Cohort study | 2017 | Weglinski et al. | Prospective evaluation of mouth and eye dryness induced by antimuscarinic drugs used for neurogenic overactive bladder in 35 patients with multiple sclerosis | Community-dwelling patients with MS, $n = 35$ with a mean age of 50.1 ± 10.2 years | Eye dryness (Xerophtalmia) Mouth dryness (Xerostomia) | | 4 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cohort study (in an intervention study) | 2018 | Jaïdi et al. | Threshold for a Reduction in Anticholinergic Burden to Decrease Behavioral and Psychological Symptoms of Dementia | Inpatients with dementia and hospitalized for behavioral and psychological symptoms (BPSD), $n=147$ with a mean age of 84.1 ± 5.2 years | Clinical and statistical significant improvement in BPSD when ACH load is reduced | + | 2a | Good | 0 | 0 | 0 | 0 |
| ADS | Cohort study (for part of outcomes) | 2018 | Sevilla-Sanchez et al. | Prevalence, risk factors and adverse outcomes of anticholinergic burden in patients with advanced chronic conditions at hospital admission | Inpatients requiring palliative care, $n = 235$ with a mean age of 86.8 ± 5.37 years | Days of hospital stay Destination after discharge Inhospital mortality 1-year survival | - - + | 2a | Good | 0 | 0 | 1 | 0 |
| ADS | Cohort study | 2018 | Tiisanoja et al. | Anticholinergic burden and dry mouth among Finnish, community-dwelling older adults | Community-dwelling, non-smoking, dentate patients, $n=152$ with a mean age of 79.4 ± 3.67 years | Xerostomia Low unstimulated salivary secretion | + + | 4 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cohort study (reanalysis on a RCT) | 2019 | Andre et al. | Anticholinergic exposure and cognitive decline in older adults: effect of anticholinergic exposure definitions in a 3-year analysis of the multidomain Alzheimer preventive trial (MAPT) study | Community-dwelling French adults, $n = 1396$ with a mean age of 75.2 ± 4.4 years | Cognitive decline (assessed with a composite score following MMSE, Free and Cued Selective Reminding Test, Category Naming Test, Digit Symbol Substitution Test) | - | 2a | Good | 0 | 1 | 0 | 0 |
| ADS | Nested Case- Control study | 2016 | Chatterjee et al. | Anticholinergic Medication Use and Risk of Fracture in Elderly Adults with Depression | Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), $n=352'937$ with depression and no baseline fractures or falls in 2007, incidence matched cohort $n=202'260$ with $n=161'808$ controls and $n=40'452$ cases, mean age of 81.4 ± 7.4 years | Fracture risk | + | 3 | Good | 0 | 0 | 0 | 0 |
| ADS | Nested Case- Control study | 2016 | Chatterjee et al. | Anticholinergic Medication Use and Risk of Dementia Among Elderly Nursing Home Residents with Depression | Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), | Dementia | + | 3 | Good | 0 | 0 | 0 | 0 |

| | | | | mpact on clinical outcomes - a systematic review, EJCP, Listach anticholinergic burden scale (ABS) (total n=147). | ibach A et al, Corresponding author: Pr Chantal Csajk | xa, Center for Research and Innovation in Clinical P | harmaceutical Sciences, | Rue du Bugnon 17, 10 | 05 Lausanne | | | | |
|-----|--|------|-----------------------|--|---|--|---------------------------|--|---------------------------|----------|-----------|----------|----------|
| ABS | Study design | | Author | Title | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | Falls |
| ADS | Nested Case- Control study | 2017 | Chatterjee et al. | Risk of Mortality Associated with Anticholinergic Use in Elderly Nursing Home Residents with Depression | Uses 2007 to 2010 Minimum Data Set linked Medicare data set from all states (US), n = 433'812 with depression, incidence matched cohort n = 224'740 with n = 179'792 controls and n = 44'948 cases, mean age of 83 years | Risk of mortality | + | 3 | Good | 0 | 0 | 1 | 0 |
| ADS | Nested Case- Control study | 2017 | Lampela et al. | Anticholinergic Exposure and Risk of Pneumonia in Persons with Alzheimer's Disease: A Nested Case-Control Study | Community-dwelling patients diagnosed with AD, cases $n=12'442$ with a mean age of 83.3 ± 6.7 years, controls $n=24'349$ with a mean age of 83.3 ± 6.5 years | Risk of pneumonia | + | 3 | Good | 0 | 0 | 0 | 0 |
| ADS | Case-Control study (multicenter) | 2018 | Aldebert et al. | Association of Anticholinergic Drug Use With Risk for Late Age-Related Macular Degeneration | Patients from 4 French ophthalmologic centers, n = 400 with cases $n = 200$ with a mean age of 74.8 ± 9.2 years and controls $n = 200$ with a mean age of 75.5 ± 7.2 years | Late Age-Related Macular Degeneration | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cross-sectional | 2012 | Drag et al. | Prescribing Practices of Anticholinergic Medications and Their Association With Cognition in an Extended Care Setting | Inpatients non-demented and non-delirious, $n=450$ with a mean age of 67.9 ± 10.5 years | Cognitive function | - | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2013 | Kersten et al. | Higher anticholinergic drug scale (ADS) scores are associated with peripheral but not cognitive markers of cholinergic blockade. Cross sectional data from 21 Norwegian nursing homes | Nursing home residents, n = 87 with a mean age of 73 years | Cognitive function (MMSE) Functional outcome (ADL) | - | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2013 | Lampela et al. | Anticholinergic Drug Use, Serum Anticholinergic Activity, and Adverse Drug Events Among Older People: A Population-Based Study | Community-dwelling, $n = 621$ with a mean age of 81.7 ± 4.9 years | Adverse events Cognitive function (MMSE, GDP) Functional outcome (ADL, IADL) | + + + + | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2015 | Moulis et al. | Exposure to Atropinic Drugs and Frailty Status | Patients attending a geriatric frailty clinic, $n = 437$ with a mean age of 83.05 ± 6.15 years | Frailty | + | 5 | Poor | 0 | 0 | 0 | 0 |
| ADS | Cross-sectional | 2017 | Ang et al. | The Impact of Medication Anticholinergic Burden on Cognitive Performance in People With Schizophrenia | Outpatients and inpatients with schizophrenia, $n = 705$ with a mean age of 39.18 ± 9.71 years | Cognitive performance (executive functions, fluency/memory, speed/vigilance) | - | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2017 | Dauphinot et al. | Anticholinergic drugs and functional, cognitive impairment and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders | Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years | Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia) | - (MMSE, NPI) - (IADL) | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2017 | Eum et al. | Cognitive burden of anticholinergic medications in psychotic disorders | Patients with schizophrenia, schizoaffective and bipolar disorders, n = 483 with a mean age 36 years | Cognitive function (BACS) if ADS ≥4 | + | 5 | Poor | 0 | 1 | 0 | 0 |
| ADS | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + - + | 5 | Poor | 0 | 1 | 0 | 1 |
| AEC | - | - | - | - | - | - | - | - | - | - | - | - | <u> </u> |
| AIS | - | - | - | - | Inpatient of 2 cohorts | - | - | - | - | - | - | - | - |
| ARS | Cohort study | 2008 | Rudolph et al. | The Anticholinergic Risk Scale and Anticholinergic Adverse Effects in Older Persons | retrospective cohort: $n = 132$ with a mean age of 78.7 ± 5.3 years prospective cohort: $n = 117$ male with a mean age of 71.5 ± 11.6 years | Central and peripheral anticholinergic adverse effects (c: falls, dizziness, confusion, p: dry mouth, dry eye, constipation) | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cohort study (multicenter) | 2011 | Kumpula et al. | Anticholinergic Drug Use and Mortality Among Residents of Long-Term Care Facilities: A Prospective Cohort Study | Hospital and long-term care, $n=1004$ ARS 0: $n=455$, with a mean age of 83.0 ± 10.0 years ARS 1-2: $n=363$, with a mean age of 80.5 ± 11.0 years ARS \geq 3: $n=186$, with a mean age of 78.7 ± 12.3 years | | - | 2a | Good | 0 | 0 | 1 | 0 |
| ARS | Cohort study (multicenter) | 2011 | Lowry et al. | Associations Between the Anticholinergic Risk Scale Score and Physical Function: Potential Implications for Adverse Outcomes in Older Hospitalized Patients | Inpatients, $n = 362$ with a mean age of 83.6 ± 6.6 years | Physical function (BI) Mortality LOS | - - - | 2a | Good | 0 | 0 | 1 | 0 |
| ARS | Cohort study | 2012 | Gouraud-Tanguy et al. | Analysis of iatrogenic risk related to anticholinergic effects using two scales in acute geriatric inpatient unit | Patients from the geriatric care unit, $n = 1379$ with a mean age of 85 ± 6 years | Total anticholinergic side effects Peripheral anticholinergic side effects Central anticholinergic side effects | + + - | 4 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2012 | Koshoedo et al. | Anticholinergic Drugs and Functional Outcomes in Older Patients Undergoing Orthopaedic Rehabilitation | Patients from a rehabilitation unit, $n=117$ with a mean age of 79 ± 7 years, with ACH $n=38$ with a mean age of 77 ± 7 years and without ACH $n=79$ with a mean age of 80 ± 6 years | Functional outcome (BI) LOS | + | 2a | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2013 | Mangoni et al. | Measures of Anticholinergic Drug Exposure, Serum Anticholinergic Activity, and All-cause Post discharge Mortality in Older Hospitalized Patients with Hip Fractures | Patients with hip fractures and planned surgery, $n = 71$ with a mean age of 84 ± 6 years | Postoperative complications LOS 3 month all-cause mortality 1 year all-cause mortality | - - + - | 2a | Good | 0 | 0 | 1 | 0 |

| - | | | | npact on clinical outcomes - a systematic review, EJCP, List ach anticholinergic burden scale (ABS) (total n=147). | bach A et al, Corresponding author: Pr Chantal Csajk | a, Center for Research and Innovation in Clinical | Pharmaceutical Sciences, | Rue du Bugnon 17, 10 | 05 Lausanne | | | | |
|-----|---|------|-----------------------|--|--|--|-------------------------------|--|---------------------------|----------|-----------|----------|---------|
| | Study design | | | Title | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | y Falls |
| ARS | Cohort study | 2014 | Dispennette et al. | Drug Burden Index score and anticholinergic risk scale as predictors of readmission to the hospital | Inpatients, n = 229 with a mean age of 78 years | Risk of hospital readmission | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2014 | Kalisch et al. | Multiple Anticholinergic Medication Use and Risk of Hospital Admission for Confusion or Dementia | Australian veterans, n = 36'015 with a mean age of 82.9 ± 6.8 years | Risk of hospitalization for confusion or dementia | + | 2b | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2014 | Kashyap et al. | Methodological Challenges in Determining Longitudinal Associations Between Anticholinergic Drug Use and Incident Cognitive Decline | Outpatient clinics without dementia or depression, $n = 102$ with a mean age of 71.9 ± 7.3 years | Cognitive function (MMSE, GDP) | + | 4 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cohort study (multicenter) | 2014 | Landi et al. | Anticholinergic Drug Use and Negative Outcomes Among the Frail Elderly Population Living in a Nursing Home | Nursing homes residents, n = 1490 with a median age of 83.56 years | Functional decline Falls Delirium | + + + + | 2a | Good | 1 | 0 | 0 | 1 |
| ARS | Cohort study | 2014 | Walter et al. | Perioperative Anticholinergic Medications and Risk of Catheterization After Urogynecologic Surgery | Female outpatients, n = 125, ACH 0-7: n = 98 with a mean age of 56.0 ± 12.1 years ACH ≥ 8 : n = 27 with a mean age of 55.3 ± 11.2 years | Failed post-operative void trial | + | 2b | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2014 | Zimmerman et al. | Increasing anticholinergic burden and delirium in palliative care inpatients | Palliative inpatients, $n = 217$ with a mean age of 72.9 ± 12.8 years | Delirium (Chart review) | + | 4 | Poor | 1 | 0 | 0 | 0 |
| ARS | Cohort study | 2015 | De La Cruz et al. | Impact of anticholinergic load on bladder function | Women undergoing urodynamics, $n = 599$, low ACH: $n = 440$ with mean age of 57.2 ± 14 years high ACH: $n = 159$ with mean age of 56.3 ± 12.9 years | Bladder function | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2015 | Lu et al. | Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study | Using the Taiwan's National Health Insurance Research Database (NHIRD), n = 59'042 aged > 65 years | All-cause admission to hospital Fracture-specific admission to hospital Death | + + - | 2b | Good | 0 | 0 | 1 | 0 |
| ARS | Cohort study | 2015 | Salahudeen et al. | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + | 2ь | Good | 0 | 0 | 0 | 1 |
| ARS | Cohort study | 2015 | Wolters et al. | I to Delimium in Critically III Patients: A Prospective Cohort | Critically ill inpatients, $n = 1112$ with a mean age of 60 ± 16 years | Delirium onset (ICU-CAM) | + | 2a | Good | 1 | 0 | 0 | 0 |
| ARS | Cohort study | 2016 | Crispo et al. | Associations between Anticholinergic Burden and Adverse Health Outcomes in Parkinson Disease | Patients with Parkinson disease, $n = 16'302 \text{ aged} \ge 40 \text{ years}$ | Delirium Fracture 30-day hospital revisits | + + + + | 2b | Good | 1 | 0 | 0 | 0 |
| ARS | Cohort study | 2016 | Mangoni et al. | Heat Waves, Drugs with Anticholinergic Effects, and Outcomes in Older Hospitalized Adults | Hospitalized patients $n=307$ in heat waves period with a median age 78 years, $n=1114$ during non heat waves period with a median age 77 years | LOS In-hospital mortality | - | 2b | Good | 0 | 0 | 1 | 0 |
| ARS | Cohort study | 2017 | Cossette et al. | Association Between Anticholinergic Drug Use and Health- Related Quality of Life in Community-Dwelling Older Adults | Community-dwelling patients free of disabilities in ADL and cognitive impairment, $n = 1793$ with a mean age of 74.4 ± 4.2 years | Mental Component Summary (MCS) Physical Component Summary (PCS) | + | 4 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cohort study | 2017 | Egberts et al. | Anticholinergic drug exposure is associated with delirium and post discharge institutionalization in acutely ill hospitalized older patients | Acutely ill, hospitalized patients (> 3 days), $n = 905$ with a mean age of 81.0 ± 7.03 years | Delirium on admission LOS Post discharge institutionalization In hospital mortality | + - + - | 2b | Good | 1 | 0 | 1 | 0 |
| ARS | Cohort study (multicenter) | 2017 | Gutierrez et al. | Anticholinergic burden and health outcomes among older adults discharged from hospital: results from the CRIME study | Inpatients total, $n = 921$ with a mean age of 81.2 ± 7.4 years ARS 0: $n = 740$ with a mean age of 80.9 ± 7.3 years ARS 1: $n = 132$ with a mean age of 82.6 ± 72 years ARS ≥ 2 : $n = 49$ with a mean age of 81.1 ± 7.8 years | Mortality within 1 year of discharge Rehospitalization within 1 year of discharge | - | 4 | Poor | 0 | 0 | 1 | 0 |
| ARS | Cohort study | 2017 | Wen-Han Hsu et al. | Comparative Associations Between Measures of Anti- cholinergic Burden and Adverse Clinical Outcomes | Inpatients n = 116'043 aged > 65 years | Emergency Department Visits All-Cause Hospitalizations Fracture-Specific Hospitalization Incident dementia | - + (for pat. <85 y.) - | 2Ь | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2018 | | Association of Anticholinergic Drug Burden with Cognitive and Functional Decline Over Time in Older Inpatients: Results from the CRIME Project | Inpatients $n = 1123$ with a mean age of 81 ± 7.5 years | Cognitive status (MMSE) Functional status (ADL) | + + | 4 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cohort study | 2018 | Clarke et al. | Association Between Objectively Measured Physical Activity and Opioid, Hypnotic, or Anticholinergic Medication Use in Older People: Data from the Physical Activity Cohort | Older people from the Physical Activity Cohort Scotland Community-dwelling, $n = 310$ with a mean age 77.3 ± 7 years | Physical activity | + | 4 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cohort study (in an intervention study) | 2018 | | Threshold for a Reduction in Anticholinergic Burden to Decrease Behavioral and Psychological Symptoms of Dementia | Inpatients with dementia and hospitalized for behavioral and psychological symptoms (BPSD), $n=147$ with a mean age of 84.1 ± 5.2 years | Clinical and statistical significant improvement in BPSD when ACH load is reduced | - | 2a | Good | 0 | 0 | 0 | 0 |

| - | | | | npact on clinical outcomes - a systematic review, EJCP, Listach anticholinergic burden scale (ABS) (total n=147). | ibach A et al, Corresponding author: Pr Chantal Csajl | xa, Center for Research and Innovation in Clinical Pl | harmaceutical Sciences, | Rue du Bugnon 17, 100 | 05 Lausanne | | | | |
|---------------|--|------|----------------------|--|--|--|---------------------------|-------------------------------------|---------------------------|----------|-----------|----------|---------|
| | Study design | | | | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortalit | y Falls |
| ARS | Cohort study | 2018 | Kose et al. | Anticholinergic load negatively correlates with recovery of cognitive activities of daily living for geriatric patients after stroke in the convalescent stage | Geriatric patients from rehabilitation center, n = 418 patients with a median age of 78 years | Functional recovery after stroke | + | 2b | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study | 2018 | Kose et al. | Assessment of aspiration pneumonia using the Anticholinergic Risk Scale | Patients from a rehabilitation ward, n = 618 with a median age of 79 years with ACH: n = 162 with a median age of 80 years and without ACH: n = 456 with a median age of 78 years | Aspiration pneumonia | + | 2b | Good | 0 | 0 | 0 | 0 |
| ARS | Cohort study (reanalysis on a RCT) | 2019 | Andre et al. | Anticholinergic exposure and cognitive decline in older adults: effect of anticholinergic exposure definitions in a 3-year analysis of the multidomain Alzheimer preventive trial (MAPT) study | Community-dwelling French adults, $n = 1396$ with a mean age of 75.2 ± 4.4 years | Cognitive decline (assessed with a composite score following MMSE, Free and Cued Selective Reminding Test, Category Naming Test, Digit Symbol Substitution Test) | - | 2a | Good | 0 | 1 | 0 | 0 |
| ARS | Nested Case- Control study | 2018 | K ose et al | Anticholinergic drugs use and risk of hip fracture in geriatric patients | Patients from a rehabilitation ward, $n = 601$ with a median age of 79 years, fracture group $n = 68$ with a median age of 80.5 years and non-fracture group $n = 533$ with a median age of 79 years | Hip fracture | + | 3 | Fair | 0 | 0 | 0 | 0 |
| ARS | Case-Control study | 2018 | • | Drugs With Anticholinergic Potential and Risk of Falls With Hip Fracture in the Elderly Patients: A Case-Control Study | Outpatients, cases $n = 300$ and controls $n = 600$ with a mean age of 81.6 years | Falls with hip fracture | + | 3 | Good | 0 | 0 | 0 | 1 |
| ARS | Cross-sectional | 2011 | Lowry et al. | Clinical and demographic factors associated with antimuscarinic medication use in older hospitalized patients | Inpatients, $n = 362$ with a mean age of 83.6 ± 6.6 years | Institutionalization and comorbidities | + | 5 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cross-sectional | 2011 | (ronhlad et al. | Use of Anticholinergic Drugs and Cholinesterase Inhibitors and Their Association with Psychological Well-Being Among Frail Older Adults in Residential Care Facilities | Nursing homes, $n = 1475$ with a mean age of 81.7 ± 7.6 years | Psychological well-being | + | 5 | Poor | 0 | 0 | 0 | 0 |
| ARS | Cross-sectional | 2013 | Bostock et al. | drug exposure and Karthel Index in older hospitalized patients | Consecutive series of community-dwelling and institutionalized settings, acute geriatric admission, $n = 271$ with a mean age of 83 ± 7 years | Barthel Index (physical function) AMT (Abbreviated Mental Test) | - | 5 | Good | 0 | 1 | 0 | 0 |
| ARS | Cross-sectional | 2013 | • | Anticholinergic Drug Use, Serum Anticholinergic Activity, and Adverse Drug Events Among Older People: A Population- Based Study | Community-dwelling, $n = 621$ with a mean age of 81.7 ± 4.9 years | Adverse events Cognitive function (MMSE, GDP) Functional outcome (ADL, IADL) | + + + + | 5 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cross-sectional | 2013 | | Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study | Hospitalized patients, $n = 1232$ with age of ≥ 65 years | Cognitive function (SBT) Physical function (BI) | + | 5 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cross-sectional | 2017 | Dauphinot et al. | Anticholinergic drugs and functional, cognitive impairment and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders | Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years | Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia) | + (MMSE, NPI) - (IADL) | 5 | Poor | 0 | 1 | 0 | 0 |
| ARS | Cross-sectional | 2017 | Mayer et al | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + + + - | 5 | Poor | 0 | 1 | 0 | 1 |
| | Cohort study | 2017 | Xu et al. | Assessing and predicting drug-induced anticholinergic risks: an integrated computational approach | Patients, exposed $n=287'614$ and unexposed $n=287'614$, with a mean age of 37.97 ± 18.79 years | Anticholinergic ADE | + | 2b | Good | 0 | 0 | 0 | 0 |
| BAADS CABS | Cross-sectional | 2017 | - Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | - - + - | 5 | Poor | 0 | 1 | 0 | 1 |
| Chew | Cohort study | 2010 | Jessen et al. | Anticholinergic drug use and risk for dementia: target for dementia prevention | Outpatients, n = 2605 and aged > 70 years | Dementia | + | 4 | Poor | 0 | 0 | 0 | 0 |
| Chew | Cohort study | 2015 | Nalahiideen et al. I | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| Chew | Cohort study | 2017 | Egberts et al. | Anticholinergic drug exposure is associated with delirium and post discharge institutionalization in acutely ill hospitalized older patients | Acutely ill, hospitalized patients (> 3 days), n = 905 with a mean age of 81.0 ± 7.03 years | Delirium on admission LOS Post discharge institutionalization In hospital mortality | - | 2b | Good | 1 | 0 | 1 | 0 |
| Chew | Cross-sectional | 2013 | - | Anticholinergic Drug Use, Serum Anticholinergic Activity, and Adverse Drug Events Among Older People: A Population- Based Study | Community-dwelling, $n = 621$ with a mean age of 81.7 ± 4.9 years | Adverse events Cognitive function (MMSE, GDP) Functional outcome (ADL, IADL) | + + + + | 5 | Poor | 0 | 1 | 0 | 0 |

| - | | | | npact on clinical outcomes - a systematic review, EJCP, List ach anticholinergic burden scale (ABS) (total n=147). | ibach A et al, Corresponding author: Pr Chantal Csajl | ka, Center for Research and Innovation in Clinical P | harmaceutical Sciences, | Rue du Bugnon 17, 1 | 005 Lausanne | | | | |
|--------------|--|------|--------------------|--|--|--|---------------------------------|--|---------------------------|----------|-----------|-------|-----------|
| | Study design | | | | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Morta | lity Fall |
| Chew | Cross-sectional | 2017 | Dauphinot et al. | clinic with subjective cognitive decline or neurocognitive disorders | Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years | Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia) | - (MMSE, NPI) - (IADL) | 5 | Poor | 0 | 1 | 0 | 0 |
| Chew | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + + + - | 5 | Poor | 0 | 1 | 0 | 1 |
| CI,PI | Cross-sectional | 2004 | Minzanhara at al I | | Outpatients with schizophrenia or schizoaffective disorders $n=106$ with a mean age of 39.9 ± 11.3 years | Simple attention Complex attention Short-term memory Delayed recall Semantic memory Working memory Executive functions Factor scores (declarative memory) | - + + + + - - | 5 | Poor | 0 | 1 | 0 | 0 |
| CrAS | Cohort study | 2001 | Han et al. | Use of Medications with Anticholinergic Effect Predicts Clinical Severity of Delirium Symptoms in Older Medical Inpatients | Inpatients with delirium, $n = 278$ with a mean age of 83.4 ± 7.3 years | Change in severity of delirium symptoms Dementia diagnosis | + | 4 | Poor | 1 | 0 | 0 | 0 |
| CrAS | Cohort study | 2008 | Han et al | Cumulative anticholinergic exposure is associated with poor memory and executive function in older men | Community-dwelling men, $n = 544$ with a mean age of 74.4 ± 5.2 years | Short term memory (HVRT) Executive function (IADL) | + + | 2a | Good | 0 | 1 | 0 | 0 |
| CrAS | Cohort study (reanalysis on a RCT) | 2009 | | Changes in anticholinergic load from regular prescribed medications in palliative care as death approaches | Palliative care patients, $n = 461$ with a mean age of 71 ± 12 years | Quality of life (McCill's Quality of life index) Functional outcome (Karnofsky performance scale) | + + | 4 | Poor | 0 | 0 | 0 | 0 |
| CrAS | Cohort study | 2009 | IIIIIAho at al | Risk Factors for Preoperative and Postoperative Delirium in Elderly Patients with Hip Fracture | Orthopedic inpatients with hip fracture, $n = 364$ with a mean age of 84 ± 4 years | Delirium (CAM, pre- and postoperatively) | - | 2a | Good | 1 | 0 | 0 | 0 |
| CrAS | Cohort study | 2010 | Clark et al. | The impact of opioids, anticholinergic medications and disease progression on the prescription of laxatives in hospitalized palliative care patients: a retrospective analysis | Palliative care, $n = 211$ with a mean age of 72.3 \pm 14.72 years | Prescription of laxatives | + | 2b | Good | 0 | 0 | 0 | 0 |
| CrAS | Cohort study | 2011 | Sheehan et sl | A Retrospective Analysis of Primary Diagnosis, Comorbidities, Anticholinergic Load, and Other Factors on Treatment for Noisy Respiratory Secretions at the End of Life | Inpatients dying in the palliative care unit, $n = 199$ with a mean age of 70.5 ± 14.8 years | Need for treatment of noisy respiratory excretions (NRS) | + | 2b | Good | 0 | 0 | 0 | 0 |
| CrAS | Cohort study | 2013 | Yeh et al. | Potential benefits of reducing medication-related anticholinergic burden for demented older adults: A prospective cohort study | Veteran home demented residents, n = 53 with a mean age of 83.4 years | Cognitive function (MMSE) Functional outcome (BI) | - | 4 | Poor | 0 | 1 | 0 | 0 |
| CrAS | Cohort study | 2015 | | Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people | Outpatients, $n = 537'387$ with a mean age of 74.7 ± 7.6 years | Hospital admissions Falls-related hospitalizations LOS GP visits | + + + + + + | 2b | Good | 0 | 0 | 0 | 1 |
| CrAS | Cross-sectional | 2017 | Dauphinot et al. | Anticholinergic drugs and functional, cognitive impairment and behavioral disturbances in patients from a memory clinic with subjective cognitive decline or neurocognitive disorders | Older outpatients visiting memory clinic, $n = 473$ with a mean age of 80.58 ± 7.48 years | Functional impairment (Functional and global cognitive performances, as well as the behavioral and psychological symptoms of dementia) | + (MMSE, NPI) - (IADL) | 5 | Poor | 0 | 1 | 0 | 0 |
| CrAS | Cross-sectional | 2017 | Mayer et al. | Comparison of Nine Instruments to Calculate Anticholinergic Load in a Large Cohort of Older Outpatients: Association with Cognitive and Functional Decline, Falls, and Use of Laxatives | Home-dwelling patients, $n = 2761$ with a mean age of 72 ± 6 years | Cognitive impairment (MMSE) Functional decline (Barthel Index) Falls Use of laxatives | + + + - + | 5 | Poor | 0 | 1 | 0 | 1 |
| DRS | Cohort study | 2015 | Hatner at al | Rating The Delirogenic Potential of Drugs for Prediction of Side Effects in Elderly Psychiatric Inpatients | Psychiatric patients with TDM, $n = 69$ with a mean age of 74.3 ± 5.7 years | Anticholinergic side effects (peripheral and central) | + | 4 | Poor | 0 | 0 | 0 | 0 |
| DS | Cohort study (multicenter) | 2017 | Rurry et al | Delirium and exposure to psychoactive medications in critically ill adults: A multi-centre observational study | Critically ill adults admitted to the ICU, $n = 520 \text{ aged} \ge 18 \text{ years}$ | Delirium (ICDSC) | + | 2a | Good | 1 | 0 | 0 | 0 |
| DS | Cohort study (multicenter) | 2017 | Gutierrez et al. | Anticholinergic burden and health outcomes among older adults discharged from hospital: results from the CRIME study | Inpatients total, $n = 921$ with a mean age of 81.2 ± 7.4 years For Duran: | Mortality within 1 year of discharge Rehospitalization within 1 year of discharge | + | 4 | Poor | 0 | 0 | 1 | 0 |
| DS | Cohort study (reanalysis on a RCT) | 2019 | Andre et al. | Anticholinergic exposure and cognitive decline in older adults: effect of anticholinergic exposure definitions in a 3-year analysis of the multidomain Alzheimer preventive trial (MAPT) study | Community-dwelling French adults, $n = 1396$ with a mean age of 75.2 ± 4.4 years | Cognitive decline (assessed with a composite score following MMSE, Free and Cued Selective Reminding Test, Category Naming Test, Digit Symbol Substitution Test) | - | 2a | Good | 0 | 1 | 0 | 0 |
| GABS KABS | - | - | - | <u>-</u> | - | - | - | - | - | - | - | - | |

| | Quality of anticholinergic burden scales and their impact on clinical outcomes - a systematic review, EJCP, Lisibach A et al, Corresponding author: Pr Chantal Csajka, Center for Research and Innovation in Clinical Pharmaceutical Sciences, Rue du Bugnon 17, 1005 Lausanne Appendix 6a: Identified validations / evaluations for each anticholinergic burden scale (ABS) (total n=147). | | | | | | | | | | | | | |
|------|--|------|------------|--|------------------|---|-------------------------|-------------------------------------|---------------------------|----------|-----------|-----------|-------|--|
| ABS | Study design | Year | Author | Title | Study population | Clinical outcome | Significant association | Evidence level (adapted EBM Oxford) | Quality (NOS, RoB 2.0) | Delirium | Cognition | Mortality | Falls | |
| SCDL | Cohort study | 2001 | Han et al. | Use of Medications with Anticholinergic Effect Predicts Clinical Severity of Delirium Symptoms in Older Medical Inpatients | 1 - | Change in severity of delirium symptoms Dementia diagnosis | - | 4 | Poor | 1 | 0 | 0 | 0 | |